AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY 108:251–260 (1999)

Genetic Evidence for Larger African Population Size During Recent Human Evolution

JOHN H. RELETHFORD[1]* AND LYNN B. JORDE[2]
[1]*Department of Anthropology, State University of New York College at Oneonta, Oneonta, New York 13820*
[2]*Department of Human Genetics, Eccles Institute of Human Genetics, University of Utah School of Medicine, Salt Lake City, Utah 84112*

KEY WORDS modern human origins; Africa; population size; microsatellite DNA

ABSTRACT Genetic evidence suggests that the long-term average effective size of sub-Saharan Africa is larger than other geographic regions. A method is described that allows estimation of relative long-term regional population sizes. This method is applied to 60 microsatellite DNA loci from a sample of 72 sub-Saharan Africans, 63 East Asians, and 120 Europeans. Average heterozygosity is significantly higher in the sub-Saharan African sample. Expected heterozygosity was computed for each region and locus using a population genetic model based on the null hypothesis of equal long-term population sizes. Average residual heterozygosity is significantly higher in the sub-Saharan African sample, indicating that African population size was larger than other regions during recent human evolution. The best fit of the model is with relative population weights of 0.73 for sub-Saharan Africa, 0.09 for East Asia, and 0.18 for Europe. These results are similar to those obtained using craniometric variation for these three geographic regions. These results, combined with inferences from other genetic studies, support a major role of Africa in the origin of modern humans. It is less clear, however, whether complete African replacement is the most appropriate model. An alternative is an African origin with non-African gene flow. While Africa is an important region in recent human evolution, it is not clear whether the gene pool of our species is completely out of Africa or predominately out of Africa. Am J Phys Anthropol 108:251–260, 1999.

Debate continues regarding the origin of anatomically modern humans. The two major viewpoints are the recent African origin model and the multiregional evolution model. The recent African origin model proposes that modern humans arose as a new species in Africa roughly 200,000 years ago and then dispersed across the Old World, replacing preexisting non-African hominid populations (e.g., Stringer and Andrews, 1988). The multiregional evolution model proposes that human evolution over the past two million years has taken place within a single evolutionary lineage of a polytypic species (e.g., Wolpoff and Caspari, 1997).

The debate over modern human origins has increasingly focused on genetic evidence. One line of evidence is the common finding that living sub-Saharan African populations have a higher level of within-group diversity than other geographic re-

Grant sponsor: NSF; Grant number: DBS-9310105; Grant sponsor: NIH; Grant number: RR-00064.

*Correspondence to: John H. Relethford, Department of Anthropology, State University of New York College at Oneonta, Oneonta, NY 13820. E-mail: relethjh@oneonta.edu

Received 5 June 1998; accepted 23 November 1998.

gions. This pattern has been found for a variety of data, including mitochondrial DNA (mtDNA) (Cann et al., 1987; Vigilant et al., 1991; Jorde et al., 1995), microsatellite DNA (Bowcock et al., 1994; Deka et al., 1995; Jorde et al., 1995, 1997; Tishkoff et al., 1996), and craniometrics (Relethford and Harpending, 1994). Preliminary analysis of Y-chromosome polymorphisms in L.B.J.'s lab suggests a similar pattern (Jorde, unpublished data). This pattern is not apparent for either classical genetic markers or restriction fragment length polymorphisms (e.g., Bowcock et al., 1994; Jorde et al., 1995). The lack of excess African diversity for these traits most likely reflects ascertainment bias (Rogers and Jorde, 1996) and a lower mutation rate (Relethford, 1997). *Alu* insertion polymorphisms also show high African diversity but slightly lower than western Asia (Stoneking et al., 1997). Apart from these exceptions, the general trend is for excess African diversity.

The evolutionary significance of these findings is less clear. Several of the early mtDNA studies suggested that excess African diversity was a reflection of a recent African origin. Diversity was considered proportional to time elapsed since a common origin. Stoneking and Cann (1989:22) noted, "If one accepts that mtDNA mutations are largely neutral, then their occurrence and accumulation are mostly a function of time: the more variability a population possesses, the older it is." This inference, combined with the suggestion of a recent coalescence for mtDNA (≈200 kyr), suggested that a recent African origin model was correct.

However, the underlying model makes the critical assumption that there was a severe bottleneck accompanying the initial dispersal out of Africa such that genetic diversity within non-African populations was "reset" (Relethford, 1995). Rogers and Jorde (1995) have shown that, unless such a severe bottleneck occurs, within-group diversity does not necessarily track a population's age. How severe does the bottleneck have to be? The critical parameter is the half-life to convergence, the number of generations for mtDNA diversity to decrease halfway toward a new equilibrium that is determined by the bottleneck population size. In order for diversity to be an index of the time since a bottleneck, the bottleneck must exist for several half-lives. Four half-lives, for example, would result in a decrease in mtDNA diversity 94% of the way to the new equilibrium. For mtDNA, the half-life is equal to N_f ln(2) generations, where N_f is the effective female population size (Rogers and Jorde, 1995). For example, it would take a bottleneck of 1,000 females 2,773 generations to reduce mtDNA diversity 94% of the way to the new equilibrium. The same value could be attained with a bottleneck of 100 females for 277 generations, 50 females for 139 generations, or 10 females for 28 generations. It does not seem reasonable to us that a bottleneck would last so long at the upper values of female population size. Nor does it seem reasonable that a population would persist more than a handful of generations at the lower values of female population size. We agree with Rogers and Jorde (1995) that regional differences in within-group diversity are not likely to tell us anything about the relative age of populations.

An alternative explanation is that within-group diversity is a reflection of demographic rather than phylogenetic history. That is, within-group diversity may reflect differences in demographic parameters (e.g., population size) rather than a history of populations branching off from a parental population. Several studies have argued that the genetic evidence could be a reflection of a larger African population size (e.g., Relethford and Harpending, 1994, 1995; Jorde et al., 1997; Stoneking et al., 1997). Higher diversity within sub-Saharan Africa is expected if the average long-term effective population size were large relative to other geographic regions. A question remains: how much larger? We would have much greater insight into ancient population dynamics if we could roughly approximate the relative population size of major geographic regions during recent human evolution. A method for estimating relative regional size was developed by Relethford and Harpending (1994) and applied to craniometric data. Their results suggest that sub-Saharan Africa accounted for roughly 50% of the total species size during recent human evolution.

More precisely, this estimate suggests that the ancestors of contemporary sub-Saharan Africans accounted for 50% of total species size, since we don't know exactly where they lived. This estimate is tentative, however, because of the potential problem of environmental influences on craniometric variation. In the present study, we extend this method to estimate relative ancient population size from patterns of genetic diversity in 60 microsatellite loci. Our results support previous suggestions of a larger long-term African population. The microsatellite data suggest that the ancestors of contemporary sub-Saharan Africans accounted for over 70% of the total species during recent human evolution.

MATERIALS AND METHODS

Our data consist of allele frequencies for 60 unlinked tetranucleotide microsatellite loci as reported by Jorde et al. (1997). These data have certain advantages over previous microsatellite analyses (e.g., Bowcock et al., 1994) that relied on fewer loci that were taken from only two chromosomes. In contrast, our loci are unlinked and chosen primarily from different chromosome arms, thereby ensuring statistical independence.

The data represent 255 individuals from 15 samples, pooled here into three major geographic regions: sub-Saharan Africa (San, Sotho/Tswana, Mbuti Pygmy, Biaka Pygmy, Tsonga, Nguni), East Asia (Malay, Vietnamese, Cambodian, Chinese, Japanese), and Europe (French, Poles, Finns, northern Europeans). Previous analysis of the allele frequencies of the 15 subsamples shows extensive clustering into these three macrogeographic regions (Jorde et al., 1997). Sample sizes by locus range from 55–72 for Africa, 52–63 for East Asia, and 105–120 for Europe. There are between three and 22 alleles per locus (defined by the number of repeats) for a total of 624 alleles. Complete details of data collection and laboratory analysis have been presented elsewhere (Jorde et al., 1997).

Heterozygosity was computed for each geographic region i and locus j as

$$H_{ij} = 1 - \sum p_{ik}^2 , \qquad (1)$$

where p_{ik} is the frequency of allele k in population i and summation is over all alleles for locus j. For each region, the average per-locus heterozygosity was computed as the average of equation 1 over all 60 loci.

The method used by Relethford and Harpending (1994) for estimating relative population size was based on an extension of the Harpending-Ward model to quantitative traits. Given allele frequency data, the same approach can be applied directly to Harpending and Ward's (1982) original model. Briefly, Harpending and Ward noted that there were two different ways to compute heterozygosity in a population. The first is from direct observation using equation 1. The second is to compute heterozygosity expected based on a population's genetic distance to the overall centroid of allele frequencies. Harpending and Ward show that the expected average per-locus heterozygosity for population i and locus j is

$$\mathrm{E}[H_{ij}] = H_{Tj}\,(1 - r_{ii}) \qquad (2)$$

where H_{Tj} is the total heterozygosity for locus j over all populations, obtained from equation 1 using the weighted mean allele frequencies over all three populations. The weighting is by relative population size. The genetic distance of population i to the weighted centroid of allele frequencies is computed for each allele as

$$\frac{(p_i - \overline{p})^2}{\overline{p}(1 - \overline{p})} , \qquad (3)$$

where p_i is the allele frequency in population i and $\overline{p}$ is the average allele frequency weighted by population size. This quantity is then averaged over all alleles and loci to estimate r_{ii} for use in equation 2. Following Relethford and Harpending (1995), we use only polymorphic alleles (those alleles whose average unweighted allele frequency over all three regions lies between 0.01 and 0.99) to compute r_{ii} (487 out of 624 alleles).

Heterozygosity can be affected by a number of factors, including time, mutation rate, population size, rates of local or regional gene flow, and rates of long-range gene flow. Harpending and Ward's (1982) method makes use of the fact that long-range gene flow will have a different effect on observed and expected heterozygosity. As such, the

TABLE 1. Regional variation of per-locus heterozygosity under the null hypothesis of equal effective population sizes

Region	Observed per-locus heterozygosity (± se)	Expected heterozygosity[1]	Residual (observed-expected) heterozygosity (± se)	P^2
Sub-Saharan Africa	0.760 (0.017)	0.729	0.032 (0.010)	0.002
East Asia	0.697 (0.021)	0.734	−0.038 (0.010)	0.000
Europe	0.732 (0.015)	0.743	−0.012 (0.006)	0.043

[1] Computed using the Harpending-Ward model under the assumption of equal effective population sizes (see text).
[2] Probability levels for a one-sample *t*-test for the null hypothesis that residual variation across loci is equal to zero (df = 59).

Harpending-Ward method provided a valuable tool by which to ascertain the effects of long-range gene flow. If long-range gene flow was the same for all populations in an analysis, then observed and expected heterozygosities should be the same. Any difference between observed and expected values provides information about differences in the rate of long-range gene flow. As shown by Relethford and Harpending (1994), the interpretation differs when considering the major geographic subdivisions of a single species. Since the entire species is a closed system, there is no long-range gene flow, and observed and expected heterozygosities should be the same. Regional differences in mutation rates is unlikely, since these differences would have to be several orders of magnitude to account for regional differences in diversity (Relethford, 1995). Any observed difference in a global analysis instead suggests that the relative population sizes used to compute average allele frequencies are incorrect. Different values of relative population size can then be entered into the model to find the combination that results in the best fit to the Harpending-Ward model.

RESULTS

Means and standard errors of observed heterozygosity are reported in Table 1. Sub-Saharan Africa shows the greatest average heterozygosity (0.760), followed by Europe (0.732) and then East Asia (0.697). Analysis of variance shows significant variation in average heterozygosity across the three geographic regions ($F = 3.15$, df = 2 and 177, $P = 0.045$). Similar results were found using the nonparametric Kruskal-Wallis test ($\chi^2 = 7.59$, df = 2, $P = 0.022$). A Bonferroni post-hoc test shows that this significant difference is due to the contrast between Africa and East Asia ($P = 0.039$). Our finding of significant heterogeneity in heterozygosity confirms an earlier analysis of allele size variation based on these data (Jorde et al., 1997).

Expected heterozygosity was computed using equations 2 and 3 under the assumption of equal regional population sizes. Expected and residual heterozygosities are reported in Table 1. These results show that the sub-Saharan African sample shows greater heterozygosity than expected, whereas both the East Asian and European samples show less heterozygosity than expected. All of these differences are statistically significant ($P < 0.05$).

Our initial results reject the null hypothesis that regional population sizes are equal. In particular, the results suggest that the long-term average population size was larger in sub-Saharan Africa and smaller in East Asia and Europe. We then turned to considering the question of what set of relative population sizes would provide the best fit to the Harpending-Ward model. Since a solution is not possible using standard regression methods, we used a "brute force" method (see also Relethford and Harpending, 1994). We repeated the analysis using all possible increments of 0.01 for relative population size in each region, subject to the constraint that the relative population sizes add up to 1 (e.g., Africa = 0.46, East Asia = 0.23, Europe = 0.31). This strategy resulted in examining 4,851 different combinations of relative population size. The lowest residual sum of squares was found with relative weights of Africa = 0.73, East Asia = 0.09, and Europe = 0.18. As shown in Table 2, residual heterozygosity is not significantly different from zero ($P \geq 0.50$) in any region when using these weights.

TABLE 2. Regional variation of per-locus heterozygosity with relative population sizes of sub-Saharan Africa (0.73), East Asia (0.09), and Europe (0.18)

Region	Observed per-locus heterozygosity (± se)	Expected heterozygosity[1]	Residual (observed-expected) heterozygosity (± se)	P[2]
Sub-Saharan Africa	0.760 (0.017)	0.763	−0.003 (0.004)	0.498
East Asia	0.697 (0.021)	0.696	0.001 (0.015)	0.974
Europe	0.732 (0.015)	0.732	−0.001 (0.010)	0.942

[1] Computed using the Harpending-Ward model using the relative effective population sizes that gave the lowest sum of squared residuals across all three regions (see text).
[2] Probability levels for a one-sample *t*-test for the null hypothesis that residual variation across loci is equal to zero (df = 59).

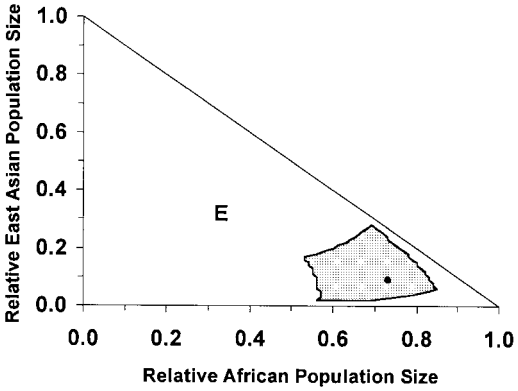

Fig. 1. Significance tests for all possible combinations of relative effective population size for Africa and East Asia based on 60 microsatellite DNA loci. Relative European effective size is the remainder (1 - Africa - East Asia). The shaded area corresponds to those combinations of relative population sizes that result in nonsignificant ($P > 0.05$) residual heterozygosity across all three geographic regions. The dot (●) indicates the combination of relative population sizes that produced the best fit to the theoretical Harpending-Ward model: Africa = 0.73, East Asia = 0.09, Europe = 0.18. E, the null hypothesis of equal population size.

Our brute force method precludes computation of standard errors for relative population size. In order to assess the possible range of relative population sizes that fit the observed data, we examined each combination of relative sizes that resulted in a nonsignificant ($P > 0.05$) average residual heterozygosity across all three geographic regions. This range, plotted in Figure 1, indicates relative African population size ranging, for the most part, between 0.6 and 0.8.

DISCUSSION

Application of the Harpending-Ward model to the analysis of global variation lends support for the hypothesis that long-term average population size of contemporary sub-Saharan Africans is larger than elsewhere in the Old World. This analysis confirms Relethford and Harpending's (1994) similar analysis using 57 craniometric traits. In that study, the relative African population size was estimated at roughly 0.5, lower than our current estimate of 0.73. This difference might be due, in part, to environmental effects on craniometrics and the fact that the craniometric analysis also included Australasia as a fourth geographic region. To compare craniometric and microsatellite analyses more closely, we repeated the Relethford-Harpending analysis using only the three geographic regions used here. Using an average heritability of 0.55 (see Relethford, 1994; Relethford and Harpending, 1994), our best fit resulted in relative population sizes of Africa = 0.57, East Asia = 0.20, and Europe = 0.23. After examining all combinations of relative sizes, we found that the range for craniometrics and microsatellite DNA overlaps, as shown in Figure 2. In other words, microsatellite DNA and craniometric data provide the same basic pattern where relative size is largest in sub-Saharan Africa.

The microsatellite analysis shows a greater relative population size for Europe than for East Asia. This regional difference is also reflected in the observed heterozygosities (Table 1), where Europe is more diverse than East Asia. This observation differs from other genetic studies that have shown lower diversity in Europe for mtDNA (Cann et al., 1987) and craniometrics (Relethford and Harpending, 1994). Several other studies of microsatellite DNA also show higher diversity in Europe than in East Asia (e.g., Bowcock et al., 1994; Tishkoff et al., 1996), although the study by Deka et al. (1995)

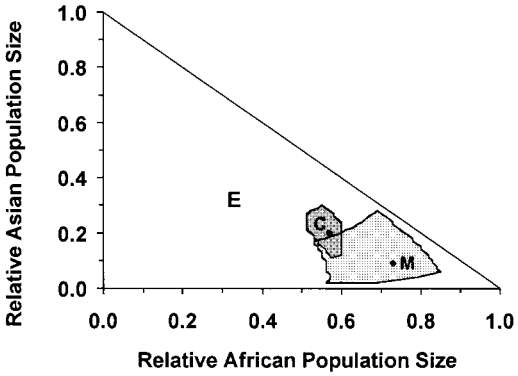

Fig. 2. Comparison of significance tests for all possible combinations of relative effective population size for Africa and East Asia based on microsatellite DNA (from Fig. 1) and craniometrics. Shaded areas correspond to those combinations of relative population sizes that result in nonsignificant ($P > 0.05$) residual heterozygosity (for microsatellite DNA) or phenotypic variation (craniometrics) across all three geographic regions. M, best fit for microsatellite DNA loci: Africa = 0.73, East Asia = 0.09, Europe = 0.18. C, best fit for craniometric data: Africa = 0.57, East Asia = 0.20, Europe = 0.23. E, the null hypothesis of equal population size. Note that the distributions for microsatellite DNA and craniometrics overlaps at a relative African population size of roughly 0.6.

shows the reverse pattern. It is not clear whether these differences are the result of ascertainment bias and/or the use of different loci and local populations. In any event, the present results show the generally consistent pattern of higher African diversity. In addition, the range of nonsignificant deviations from the Harpending-Ward model includes cases where Asia has a higher relative weight than Europe (Fig. 1).

Our application of the Harpending-Ward model assumes that we are working on a global level and sampling enough of the species so that residual heterozygosity reflects specification in relative population size and not differences in gene flow from a region not included in the analysis. We doubt that inclusion of other regions (e.g., Australasia) would have much effect on the overall finding of larger sub-Saharan African population size. For example, our current analysis of craniometric variation suggests a relative African size of 0.57, not appreciably different from the previous estimate of 0.5 when Australasia was included (Relethford and Harpending, 1994). While not definitive, this analysis suggests that while the exact relative size could be affected by the inclusion of other regions, the net effect of larger African size remains.

What do these findings tell us about modern human origins? The finding that sub-Saharan Africa has the largest long-term average effective population size does not translate directly into support for one model vs. another. It is important to understand exactly what is meant by a long-term effective population size. Population genetics frequently uses effective population size to represent complex population dynamics in terms of a single number. As such, a long-term effective size is an average population size over time. As shown by Sewall Wright (1938), average effective size over time is described better by a harmonic mean than by an arithmetic mean. For example, if a small population expands later in time, then the long-term effective population size will be much closer to the minimum size than to the arithmetic average or the maximum size.

Any estimate of long-term effective size could easily mask a wide range of complex demographic histories. The same is true when comparing relative long-term effective size across different geographic regions. The observation that sub-Saharan Africa has the largest long-term average effective size could result from many possible demographic scenarios. Was Africa always larger? Did it expand in size more quickly, or earlier, than other regions? Did other regions expand earlier but later decline in size? The problem with analyses such as ours is that they tell us only about the net outcome of demographic and evolutionary events, not the detailed history of such events.

In spite of this problem, some clues are available from other methods and sources of data. Analyses of the mismatch distributions of mtDNA suggest that the human species expanded rapidly in size roughly 50,000 years ago (Rogers and Harpending, 1992; Harpending et al. 1993; Sherry et al. 1994; Rogers, 1995, 1997; Rogers and Jorde, 1995). If so, then the larger African long-term effective population size could be the result of Africa being larger before the expansion and/or Africa expanding earlier than

other regions. Evidence to date suggests that both factors are responsible: Africa was larger before the expansion and expanded in size somewhat earlier than other regions (Relethford, 1998b).

These findings are also supported by recent analyses of microsatellite DNA. Both Kimmel et al. (1998) and Reich and Goldstein (1998) found evidence for an African expansion using part or all of the same data set reported here. While Reich and Goldstein found no evidence for a non-African expansion, their analysis was based on a subset of 30 microsatellite loci. Kimmel et al. (1998) used the same 60 loci as reported here and found evidence of both African and non-African population expansions with further suggestion of an earlier African expansion. Di Rienzo et al. (1998) analyzed a different set of microsatellite DNA data and also found evidence for expansion across the Old World with the suggestion of an earlier expansion in Africa.

There are two different ways to interpret these findings. Under the "weak Garden of Eden" model proposed by Harpending et al. (1993), the human species arose in Africa roughly 200,000 years ago. Regional populations remained small and relatively isolated until the Late Pleistocene, at which point they all increased in size relatively quickly. Given Africa as the parent population, we would expect it to be initially larger than founding populations in other regions, which is consistent with estimates of pre-expansion mtDNA diversity (Relethford, 1998b). Preliminary estimates also suggest that Africa expanded in size earlier than other regions based on mtDNA (Sherry et al., 1994; Relethford, 1998b) and microsatellite DNA (Kimmel et al., 1998). Either or both of these factors would result in a larger African long-term effective population size under this variant of the recent African origin model.

While a recent African origin model is compatible with our results, this does not constitute proof, since a larger African effective size is also compatible with the multiregional evolution model. Under the multiregional model, Africa was an evolutionary center and is expected to have been larger in size than regional populations on the periphery of human distribution (Wolpoff and Caspari, 1997). From a geographic point of view, Africa had the greatest amount of usable land mass and is expected to have been larger until very recently in human prehistory (Thorne et al., 1993; Wolpoff and Caspari, 1997). The possibility of a long history of larger African size is also supported by the fossil record. Thorne and Wolpoff (1981) found evidence of higher levels of phenotypic diversity in African *Homo erectus* as compared with Asian *Homo erectus*, as expected from larger African population size.

Since a larger long-term African population is compatible with both origin models, resolution of the debate must rest on other genetic evidence. The fact that genetic evidence is compatible with an African replacement does not necessarily mean that this model is correct, since much evidence can also be interpreted under a multiregional framework (Relethford 1995, 1998a). Perhaps the strongest evidence supporting African replacement is the finding, based on many different traits, that the long-term effective population size of our species is roughly 10,000. This small size has generally been viewed as too small to allow a species to have been spread over three continents for close to two million years and remain connected by gene flow. The small species size appears to be incompatible with a multiregional model (Harpending et al., 1993, 1998; Rogers and Jorde, 1995; Jorde et al., 1998).

This conclusion rests upon the assumption that total census population size is also very low. Assuming that roughly half of a hunting-gathering society is of reproductive age implies that an effective population size of 10,000 is roughly equivalent to a census population size of 20,000, which would be too few individuals to have been spread across the Old World. However, other factors might have operated to produce a small *effective* population size in a species with a moderately large *census* size. The most relevant of these is the process of local population extinction, where small local groups become extinct and are replaced by colonists from a nearby population. Local extinction

and recolonization can drastically reduce the ratio of effective size to census size when migration is low relative to extinction (Maryuma and Kimura, 1980; Takahata 1994; Whitlock and Barton, 1997).

Relatively low migration rates, however, will lead to increased differentiation among populations, which in turn increases effective population size (Nei and Takahata, 1993). At first glance, it would seem that any reduction in effective population size due to local extinction would be offset by an increase in differentiation among groups. However, when local extinction and increased differentiation are both present, then the net result can be a dramatic decrease in effective population size (Whitlock and Barton, 1997). One of us (J.H.R.) is currently working with these models to infer the magnitude of such effects in recent human evolution. For the present, however, we simply note that extinction of small local populations and increased fragmentation and differentiation of populations would be expected given what we know of environmental conditions during much of the Pleistocene. It remains possible that the low effective size of our species is compatible with a census population large enough to encompass parts of at least two continental regions. We view the resolution of this problem as critical in distinguishing between complete African replacement or a model that incorporates an African origin with non-African gene flow.

While many genetic studies have provided results that are compatible with an African replacement, analyses of beta-globin alleles (Harding et al., 1997) and Y-chromosome haplotypes (Hammer et al., 1998) suggest Asian contributions to the gene pool of living humans. If confirmed, these results, combined with the other evidence discussed above, suggest the possibility of an African origin combined with genetic input from at least one other region: Asia. It is interesting in this regard that the fossil evidence suggested for regional continuity is argued to be strongest in East Asia and Australasia (e.g., Wolpoff, 1989).

What conclusions can be made at this point? We feel that the genetic evidence in the present study and elsewhere argues for a dominant role of Africa in the origin of modern humans. It is less clear, however, whether *only* Africa was involved in the transition from archaic to modern humans; it seems possible that there has been some non-African admixture (Jorde et al., 1998). If true, several questions come to mind concerning the geographic distribution and nature of such admixture. If there was genetic input from non-African populations, how many and which ones were involved? Was this gene flow in the form of invasion with admixture or gene flow across a polytypic species? If complete replacement can be ruled out, then the next step is determining the nature of non-African gene flow.

Finally, there is also the question of how a primary but not exclusive African origin fits into traditional arguments and previous hypotheses over modern human origins. The multiregional model is frequently portrayed as postulating genetic input from all major geographic regions and further requiring that genetic input be greatest within each region. This portrayal is incorrect. In the most general sense, multiregional evolution requires only that there be some genetic input from outside of Africa, not necessarily from all regions outside of Africa (Relethford, 1998a; Wolpoff, 1998). Models that propose a primary role for Africa with some non-African gene flow (e.g., Bräuer, 1984; Smith et al., 1989) are often viewed as intermediate models, but in fact they are specific variants of the general multiregional model (for a good discussion on variants within the general model see Wolpoff et al., 1994).

Our analyses suggest a primary role of Africa in the evolution of modern humans. Further genetic and paleoanthropological studies are needed to resolve whether other geographic regions were involved and whether the origins of modern humans can best be described in terms of replacement or multiregional evolution. If the latter, then further work will be needed to clarify the relative roles of each major geographic region. Regardless of which model is correct, we suggest that our recent African ancestors contributed a majority of our current ancestry. In that sense, the origin of modern humans might be thought of as "mostly out of Africa."

ACKNOWLEDGMENTS

We thank Michael Bamshad, Henry Harpending, Alan Rogers, and Scott Watkins for their assistance. This research was supported in part by NSF grant DBS-9310105 and NIH grant RR-00064, both awarded to L.B.J.

LITERATURE CITED

Bowcock AM, Ruiz-Linares A, Tomfohrde J, Minch E, Kidd JR, Cavalli-Sforza LL. 1994. High resolution of human evolutionary trees with polymorphic microsatellites. Proc Natl Acad Sci U S A 368:455–457.

Bräuer, G. 1984. A craniological approach to the origin of anatomically modern *Homo sapiens* in Africa and implications for the appearance of modern Europeans. In: Smith FH, Spencer F, editors. The origins of modern humans: a world survey of the fossil evidence. New York: Liss. p 327–410.

Cann RL, Stoneking M, Wilson AC. 1987. Mitochondrial DNA and human evolution. Nature 325:31–36.

Deka R, Jin L, Shriver MD, Yu LM, DeCroo S, Hundrieser J, Bunker CH, Ferrell RE, Chakraborty R. 1995. Population genetics of dinucleotide $(dC\text{-}dA)_n \cdot (dG\text{-}dT)_n$ polymorphisms in world populations. Am J Hum Genet 56:461–474.

Di Rienzo A, Donnelly P, Toomajian C, Sisk B, Hill A, Petzl-Erler M, Haines GK, Barch DH. 1998. Heterogeneity of microsatellite mutations within and between loci, and implications for human demographic histories. Genetics 148:1269–1284.

Hammer MF, Karafet T, Rasanayagam A, Wood ET, Altheide TK, Jenkins T, Griffiths RC, Templeton AR, Zegura SL. 1998. Out of Africa and back again: Nested cladistic analysis of human Y chromosome variation. Mol Biol Evol 15:427–441.

Harding RM, Fullerton SM, Griffiths RC, Bond J, Cox MJ, Schneider JA, Moulin DS, Clegg JB. 1997. Archaic African *and* Asian lineages in the genetic ancestry of modern humans. Am J Hum Genet 60:772–789.

Harpending HC, Ward RH. 1982. Chemical systematics and human populations. In: Nitecki M, editor. Biochemical aspects of evolutionary biology. Chicago: University of Chicago Press. p 213–256.

Harpending HC, Sherry ST, Rogers AR, Stoneking M. 1993. The genetic structure of ancient human populations. Curr Anthropol 34:483–496.

Harpending HC, Batzer MA, Gurvens M, Jorde LB, Rogers AR, Sherry ST. 1998. Genetic traces of ancient demography. Proc Natl Acad Sci U S A 95:1961–1967.

Jorde LB, Bamshad MJ, Watkins WS, Zenger R, Fraley AE, Krakowiak PA, Carpenter KD, Soodyall H, Jenkins T, Rogers AR. 1995. Origins and affinities of modern humans: a comparison of mitochondrial and nuclear genetic data. Am J Hum Genet 57:523–538.

Jorde LB, Rogers AR, Bamshad M, Watkins WS, Krakowiak PA, Sung S, Kere J, Harpending HC. 1997. Microsatellite diversity and the demographic history of modern humans. Proc Natl Acad Sci U S A 94:3100–3103.

Jorde LB, Bamshad M, Rogers AR. 1998. Using mitochondrial and nuclear DNA markers to reconstruct human evolution. Bioessays 20:126–136.

Kimmel M, Chakraborty R, King JP, Bamshad M, Watkins WS, Jorde LB. 1998. Signatures of population expansion in microsatellite repeat data. Genetics 148:1921–1930.

Maryuma T, Kimura M. 1980. Genetic variability and effective population size when local extinction and recolonization of subpopulations are frequent. Proc. Natl. Acad. Sci. U S A 77:6710–6714.

Nei M, Takahata N. 1993. Effective population size, genetic diversity, and coalescence time in subdivided populations. J Mol Evol 37:240–244.

Reich DE, Goldstein DB. 1998. Genetic evidence for a Paleolithic human population expansion in Africa. Proc Natl Acad Sci U S A 95:8119–8123.

Relethford JH. 1994. Craniometric variation among modern human populations. Am J Phys Anthropol 95:53–62.

Relethford JH. 1995. Genetics and modern human origins. Evol Anthropol 4:53–63.

Relethford JH. 1997. Mutation rate and excess African heterozygosity. Hum Biol 69:785–792.

Relethford JH. 1998a. Genetics of modern human origins and diversity. Annu Rev Anthropol 27:1–23.

Relethford JH. 1998b. Mitochondrial DNA and ancient population growth. Am J Phys Anthropol 105:1–7.

Relethford JH, Harpending HC. 1994. Craniometric variation, genetic theory, and modern human origins. Am J Phys Anthropol 95:249–270.

Relethford JH, Harpending HC. 1995. Ancient differences in population size can mimic a recent African origin of modern humans. Curr Anthropol 36:667–674.

Rogers AR. 1995. Genetic evidence for a Pleistocene population explosion. Evolution 49:608–615.

Rogers AR. 1997. Population structure and modern human origins. In: Donnelly P, Tavaré S, editors. Progress in population genetics and human evolution. New York: Springer-Verlag. p 55–79.

Rogers AR, Harpending H. 1992. Population growth makes waves in the distribution of pairwise genetic differences. Mol Biol Evol 9:552–569.

Rogers AR, Jorde LB. 1995. Genetic evidence on modern human origins. Hum Biol 67:1–36.

Rogers AR, Jorde LB. 1996. Ascertainment bias in estimates of average heterozygosity. Am J Hum Genet 58:1033–1041.

Sherry ST, Rogers AR, Harpending H, Soodyall H, Jenkins T, Stoneking M. 1994. Mismatch distributions of mtDNA reveal recent human population expansions. Hum Bio. 66:761–775.

Smith FH, Falsetti AB, Donnelly SM. 1989. Modern human origins. Yrbk Phys Anthropol 32:35–68.

Stoneking M, Cann RL. 1989. African origin of human mitochondrial DNA. In: Mellars P Stringer C, editors. The human revolution: behavioral and biological perspectives on the origin of modern humans. Princeton: Princeton University Press. p 17–30.

Stoneking M, Fontius JJ, Clifford SL, Soodyall H, Arcot SS, Saha N, Jenkins T, Tahir MA, Deininger PL, Batzer MA. 1997. *Alu* insertion polymorphisms and human evolution: evidence for a larger population size in Africa. Genome Res 7:1061–1071.

Stringer CS, Andrews P. 1988. Genetic and fossil evidence for the origin of modern humans. Science 239: 1263–1268.

Takahata N. 1994. Repeated failures that led to the eventual success in human evolution. Mol Biol Evol 11:803–805.

Thorne AG, Wolpoff MH. 1981. Regional continuity in Australasian Pleistocene hominid evolution. Am J Phys Anthropol 55:337–349.

Thorne AG, Wolpoff MH, Eckhardt RB. 1993. Genetic variation in Africa. Science 261:1507–1508.

Tishkoff SA, Dietzsch E, Speed W, Pakstis AJ, Kidd JR, Cheung K, Bonné-Tamir B, Santachiara-Benerecetti

AS, Moral P, Krings M, Pääbo S, Watson E, Ritsch N, Jenkins T, Kidd KK. 1996. Global patterns of linkage disequilibrium at the CD4 locus and modern human origins. Science 271:1380–1387.
Vigilant L, Stoneking M, Harpending H, Hawkes K, Wilson AC. 1991. African populations and the evolution of human mitochondrial DNA. Science 253:1503–1507.
Whitlock MC, Barton NH. 1997. The effective size of a subdivided population. Genetics 146:427–441.
Wolpoff MH. 1989. Multiregional evolution: the fossil alternative to Eden. In: Mellars P, Stringer C, editors. The human revolution: behavioral and biological perspectives on the origin of modern humans. Princeton: Princeton University Press. p 62–108.
Wolpoff MH. 1998. Concocting a divisive theory. Evol Anthropol 7:1–3.
Wolpoff MH, Caspari R 1997. Race and human evolution. New York: Simon and Schuster.
Wolpoff MH, Thorne AG, Smith FH, Frayer DW, Pope GG. 1994. Multiregional evolution: a world-wide source for modern human populations. In: Nitecki MH, Nitceki DV, editors. Origins of anatomically modern humans. New York: Plenum Press. p 175–199.
Wright S. 1938. Size of population and breeding structure in relation to evolution. Science 87:430–431.